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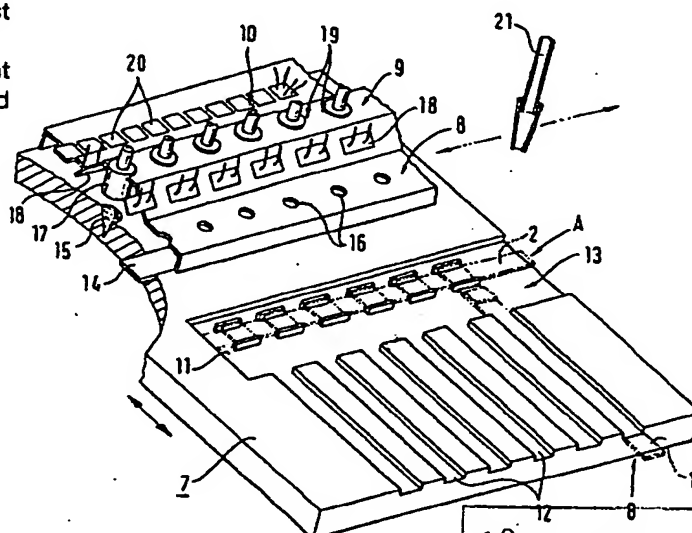
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(54) A method for analyzing special component in liquid.

(57) In the invention, an apparatus having photometric part, wherein plural light receiving parts were sideways arranged with specified space, is used and both of multi-item test piece and single item test piece can be used.

Multi-item test piece is fed sideways to light receiving part, and single item test piece is fed lengthways to light receiving part.

Fig. 2



EP 0 286 101 A2

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SEARCH REPORT

## A method for analyzing special component in liquid

### Background of the Invention

This invention relates to improvement of a method and apparatus for analyzing special component in liquid wherein body fluid, particularly blood, is analyzed and measured chemically by the use of the analytical test piece with reagent layer containing reagent, particularly to a method, apparatus, and test piece whereby necessary items can be measured simply, rapidly, and without erroneous operation by separately using multi-item test piece able to measure at one time multiple items or single item of plural samples and single item test piece for measuring single item of single sample.

The technology for analyzing the presence, quantity, or change of special component in blood (plasma, serum, whole blood) has made great progress along with rapid improvement of reagent and analyzing apparatus, and by combination of single item measurement such as a glucose concentration and the information of multiple components the diagnosis of various diseases or organs disorders and synthetic health examination have been generally made to help the treatment.

For example, by set test of GOT, GPT, ALP, LAP,  $\gamma$ -GTP, and BUN in blood the diagnosis of liver disorders is conducted. To assess synthetically the health of patient in the first examination, blood sugar, creatinine, uric acid, BUN, cholesterol, TP, amylase, LDH, and GOT are analyzed as a profile test. In set examination, there are the combination analysis of glucose, BUN, total cholesterol, creatinine, uric acid, and inorganic phosphorus for the diagnosis of renal function and the combination of glucose, total protein, BUN, total cholesterol, and uric acid for the diagnosis of diabetes. As measurement items other than the above, there are bilirubin, albumin, cholinesterase, triglyceride, CPK, calcium, HBDH, ACP, lipase, serum iron, and lactic acid.

For conducting readily these analysis as a bedside test for in-patients or as a real time test for out-patients, a dry system using a test piece containing a reagent layer is the most appropriate. The reagent layer is prepared by sticking filter paper impregnated by reagents on a support or by drying after applying reagents to a support (strip etc.).

However, to conduct a set test or a profile test in a short time, the concurrent reaction and measurement of plural test piece are necessary, resulting in problems such as complexity of operation or a combination mistake leading to erroneous judgement. In case of a large number of samples, the

operation is more difficult.

As a means against the above problems, the adoption of multi-item test piece with plural layers of different reagents on one test piece is considered. In fact, in urine, multi-item test piece has been used since ago. However, in urine, measurement items are several to ten at most, covered by one to two multi-item test piece.

On the contrary, in the blood, the number of measurement items are 25-60, and all measurement can not be conducted by 1-2 of test piece. In addition, preparing multi-item test piece for each item necessary for the diagnosis or course observation of every disease is impossible in view of the cost or control in practice.

On the other hand, though several types of multi-item test piece are prepared limited to the presentative diseases, the necessity of measuring items lacking in the combination occurs inevitably, resulting in the increase of types of necessary test piece. Further, in the case of the measurement of a particular item, the multi-item test piece is used wastefully. This problem may be solved by using together with single item test piece, but exclusive measurement apparatus for each piece is necessary, resulting in defects in view of the cost, place, treatment, and reliability of data owing to the difference of apparatus.

### Summary of the Invention

The invention has the object of solving the above problems, and has the object of conducting rapidly test  $\rightarrow$  diagnosis  $\rightarrow$  treatment by practicing the measurement of multiple items such as a set or profile test readily in a short time. Further, the invention has the object of providing a method and apparatus for obtaining correct measurement values by preventing erroneous diagnosis owing to the mistake of test piece in measurement.

In addition, the invention has the object of providing a method and apparatus for conducting rapidly single item measurement of multiple samples.

To attain these objects, the invention is so constructed as to be able to measure multi-item test piece and single item test piece for the supplement or single test of a special item in the same apparatus to measure multiple special components in blood sample. Besides, multi-item test piece with plural layers of same reagents can be used for the test of special item of multiple samples.

A photometric part wherein plural measuring means composed of a light source part and a light

receiving part are arranged sideways with a specified space is used, and multi-item test piece is fed to the photometric part sideways so that each reagent layer of the same test piece applied sample is separately observed at the corresponding light receiving part.

#### Brief Description of the Drawings

Fig.1 shows an example of test piece used in the invention, Fig.1 (a) showing single item test piece, Fig.1 (b) multi-item test piece.

Fig.2 is a rough oblique drawing showing an example of the main parts of the invention, Fig.3, Fig.4, and Fig.5 show the rough drawings of the different apparatus, Fig.3 and Fig.4 are plans, and Fig.5 is an oblique.

#### Detailed Description of the Invention

The method of the invention is to measure the multiple items of a sample using both of multi-item test piece and single item test piece.

By the use of multi-item test piece with plural reagent layers for specified items, the specified items of sample are analyzed, and for the supplement the other one or plural items are measured by the use of single item test piece. By the use of the method, all items are covered by preparing multi-item test piece in combination to some extent and by preparing single item test piece for the other items. In addition, measuring operation and times are remarkably shortened compared with the case wherein all items are analyzed by single item test piece.

Further, the method of the invention can be also used in the analysis of one item in multiple samples. For example, in the case of measurement of the same item in 7 samples, 6 samples are analyzed by multiple items test piece (in this case test piece with 6 layers of the same reagent), and one residual sample is analyzed by single item test piece.

Thus, without a wasteful use of multi-item test piece, similarly with the above mentioned, measuring operation and times are shortened compared with the case wherein all items are analyzed by single item test piece.

The apparatus of the invention will be described in the following. The apparatus of the invention is not only used for the above-mentioned method of the invention, but also used for the measurement of multiple items of multiple samples.

Fig.1 shows an example of test piece of the invention. Fig.1 (a) and (b) show single item test

piece 1 and multi-item test piece 2 respectively. In single item test piece 1, one reagent layer is fixed on the end of the stick 4, a bar-code is put on the center as test piece judgement means, and the notation 6 of measuring substance is put near the base. For example, the bar-code is composed of start bits(S1, S2), data bits(D1, D2, ... D7), and a parity bit(P). Stick 4 is, for example, transparent plastic sheet cut to ca 5 mm width.

On the other hand, in multi-item test piece, plural(6 in Fig.1 (b)) reagent layers 3a, 3b ... 3f impregnated reagents react with each different substance are fixed in order with a specified space from the end of the stick 4, and the names of plural measurable substances of the notation 6 of diseases measurable with the combination are written near the base. As means of judgement of test piece, bar-codes 5a, 5b, ... 5e are put between each reagent layer 3a, 3b ... 3f, but in this example only one data bit on each position is put because of the reading direction. The bar-codes 5a ... may be only mark, that is, by the presence of the mark between each reagent layer the type of multi-item test piece is judged. Since 32 types of test piece are discriminated by 5 positions of mark, even such simple mark notation is useful sufficiently.

Fig.2 shows roughly the main part of the invention apparatus composed of a movable test piece table 7 long in length, a sample liquid applying part 8 fixed covering the part of the test piece table 7 on the upper part of the table, a photometric part 9, and a test piece judging part 10.

On the test piece table 7, a lateral groove 11 for setting a multi-item test piece 2 and plural(6 in Fig.) longitudinal grooves 12 ... for setting single item test pieces 1 are provided. The lateral groove 11 is provided nearly on the center of the test piece table 7 parallel with the photometric part 9. The longitudinal grooves 12 are provided on the positions corresponding to the positions of the reagent layers of test piece 2 set on the lateral groove 11 vertical to 11.

On the position of the lateral groove 11 and the head of the longitudinal groove 12, that is the position of each pad 3, 3a, 3b ... of test pieces, heaters are set as constant temperature zone 13.

On the front of the lateral groove 11, a standard reflex piece of white ceramic plate 14 and plural(6 in the example) black damping cylinder 15 are provided. These are for the correction of reflectivity, which is conducted as the former of reflectivity 100% and the latter of reflectivity 0%, that may be a black plate.

The sample liquid applying part 8, the photometric part 9, and the test piece judging part 10 are all together closely fixed at the upper part of the test piece table 7, being useful in keeping temperature as the constant temperature zone 13.

The sample liquid applying part 8 is a plate of small width provided eyeholes 16 ... at the position of the reagent layer of each test piece.

In the photometric part 9, plural(6 in Fig.) measurement devices 19 of combination of the light source part 17 and the light receiving part 18 are arranged sideways. The light source part 17 radiates light(multi-wavelength) from the light source-(omission in Fig.) on each reagent layer, in the example the end of light fiber(light-guide) being set over the position of the reagent layer. The light receiving part 18 receives light reflecting from the reagent layer, composed of a light detector. As a measurement device 19, an integrating sphere or the other device may be also usable.

The test piece judging part 10 reads the bar-code of each test piece, arranged sideways plural(11 in Fig.) measurement devices 20 ... composed of the photo-interruptor of combination of a luminous diode and a photo-transistor. The measurement devices 20 are more than the measurement devices 19 of the photometric part 9, because the positions of bar-code 5, 5a ... shift according to multi-item test piece or single item test piece. The measurement device 20 may be composed of a light-guide and a light detector.

The test piece judging part 10 may be positioned forer than the sample liquid applying part 8.

The analysis procedure of blood sample by the invention apparatus will be described in the following.

First, a multi-item test piece 2 is set on the lateral groove 11. (the state in Fig.2 A) Next, the test piece table 7 is made a large straight advance to send the test piece 2 to the position of the test piece judging part 10, and bar-codes 5a, 5b ... 5e are read to judge the type of the test piece 2, and the type of measurement of each reagent layer 3a, 3b ... 3f (end-point method, rate method) and the time from reaction to measurement start are determined based on the data memorized by micro-computer (omission in Fig.). At the same time, the surface of each reagent layer is observed, and if a wet surface is found, it may be cancelled as measured.

Next, the test piece table 7 is made back to bring the test piece under the sample liquid applying part 8, and the same sample is applied to each reagent layer 3a, 3b ... by a nozzle 21 from a sample vessel(omission in Fig.) set in advance. After applying the test piece table 7 is a little made forward, and after specified time the reflectivity of each reagent layer is measured.

Before measurement the reflectivity of each measurement device 19 is corrected by the standard reflectivity piece 14 and the black damping cylinder 15. Obtained data are memorized in microcomputer and output in output device(omission

in Fig.) converted to the concentration or the other measurement value based on the calibration data memorized in advance. After finishing measurement the test piece is removed and a new multi-item test piece 2 is prepared and a similar test is continued.

According to the state of patient, in case necessary measurement items are satisfied, the measurement is finished at this point. In case there are plural samples, the test piece is removed after finishing measurement, a new multi-item test piece is prepared, similar operation is continued.

In case measurement items are not satisfied with one type of multi-item test piece 2, a single item test piece 1 in accordance with the lacking item(possible till 6 items in this example) is put on the longitudinal groove 12 (the state in Fig.2 B). Next, similarly the judgement of the test piece, sample liquid application, and measurement are conducted. Multi-item test piece 2 and single item test piece 1 may be set at the same time on each groove 12, 12 ... and measured continuously.

Single item test piece is also used for screening tests wherein an item(may be 2~3 items) on multiple samples is measured. In the case of many samples, the use of multi-item test piece with the same reagent layer 3a, 3b ... remarkably simplifies the measurement operation.

On the form and movement of the test piece table 7, the other varieties are considered. For example, 2 or more of the lateral groove 11, 11 as Fig.3 or the lateral groove 11 made oblique as Fig.4 are considered. In the former, plural multi-item test pieces 2 can be set at the same time, and continuous treatment of multiple samples or multi-item measurement with different test pieces 2 is simplified. In the latter, test piece 2 is easily set. Fig.5 shows a test piece table 7 of disk type, which is so constructed that test piece setting, judgement, measurement, and removal are conducted in order by several groups of the set of the lateral groove 11 and the longitudinal groove 12 ..., being suited for multiple sample treatment.

In examples above-mentioned, the longitudinal grooves 12 ... set single item test piece are positioned in agreement with each reagent layer 3a, 3b ... of multi-item test piece set on the lateral groove 11. However, the space between each longitudinal groove 12 may be made independent of the pitch of each reagent layer 3a, 3b ..., and any number of the longitudinal groove may be provided. In this case, the photometric part 9, each measurement device 19 ..., 20 ... of the test piece judging part 10, and the eyeholes 16 ... of the sample liquid applying part 8 are provided by the number of reagent layer of each test piece 1, 2. If each longitudinal groove 12 ... is shifted sideways to agree with the position of the bar-code of multi-

item test piece 2, 11 of the measurement devices 19 and the eyeholes 16 and 6 of the measurement device 20 meet the purpose.

Further, as a means for judging each test piece, in place of bar-code, color indication, eyehole, or notch may be provided by using the corresponding detecting means, or each reagent layer may be observed by transmitted light or fluorescence in place of reflected light.

As mentioned above, the invention provides a method and apparatus, wherein both types of single and multi-item test piece can be measured in one apparatus. To the photometric part wherein plural light receiving parts are sideways arranged with specified space, in the case of a multi-item test piece, each reagent layer applied sample of the same test piece is fed sideways to the corresponding light receiving part, and in the case of a single item test piece, the reagent layer applied sample of each test piece is fed lengthwise to the corresponding light receiving part.

Accordingly, in the case of multi-item test such as a set test of various diseases or a profile test in a new patient, the test is conducted readily and rapidly without the problem of wrong diagnosis owing to the mistake of test piece, avoiding the reexamination of patient, resulting in the decrease of medical cost. Further, also in single item measurement, by using multi-item test piece with plural pads of the same type, multiple samples are rapidly treated. The invention method has a large effect by meeting user's various requirements.

#### Claims

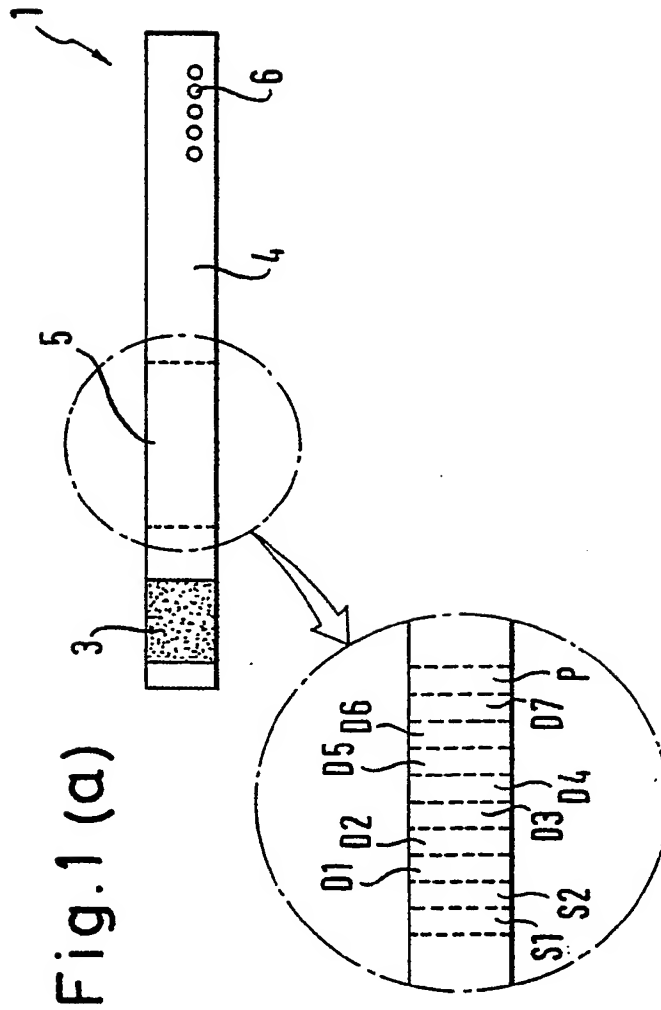
1. A method for analyzing special component in liquid, wherein both of single and multi-item test piece are used, and to a photometric part wherein plural light receiving parts are sideways arranged with specified space, multi-item test piece is fed with each reagent layer applied sample of the same test piece facing sideways to the corresponding light receiving part, and single item test piece is fed with the reagent layer applied sample of each test piece facing lengthways to the corresponding light receiving part, and reflected light is measured in the photometric part, whereby the concentration of special component is measured.

2. An apparatus for analyzing special component in liquid comprising a photometric part wherein plural measurement means comprising light source part and light receiving part are sideways arranged with specified space, a test piece table positioned under the photometric part wherein 1~several places for setting multi-item test piece nearly parallel to the photometric part and 1~several places for setting single item test piece

nearly along the moving direction of the table were prepared, and a moving means for moving the test piece table before and behind to move between the position for setting the test piece and the position for photometry of the reagent layer.

3. An apparatus for analyzing special component in liquid comprising a photometric part wherein plural measurement means comprising light source part and light receiving part are sideways arranged with specified space, a table of disk type positioned under the photometric part supported rotatably, and a means for rotating the table intermittently, and on the said table 1~several multi-item test piece setting places prepared radially and at least one group of 1~several single item test piece setting places nearly crossing at right angles with the said multi-item test piece setting places were prepared.

4. A test piece for measuring multi-item having plural reagent layers, wherein a mark for discriminating the type of the test piece is printed at least on one place of the piece.



**Fig.1(b)**

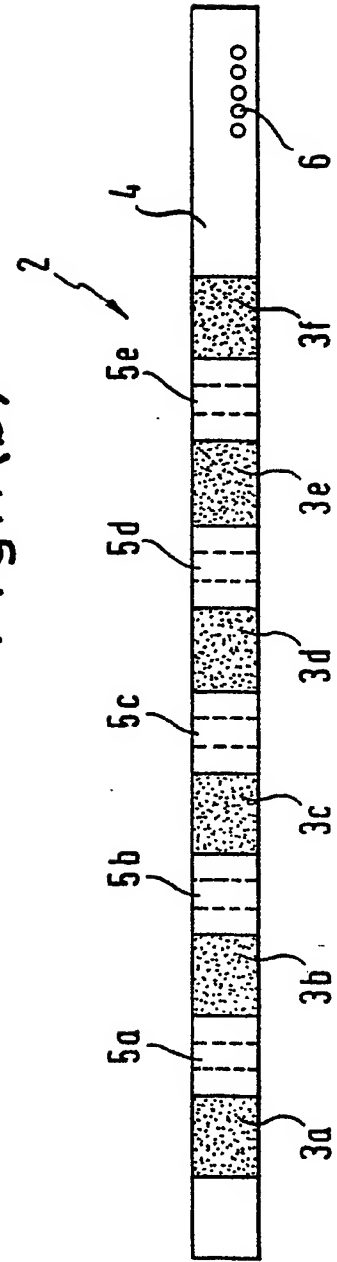


Fig. 2

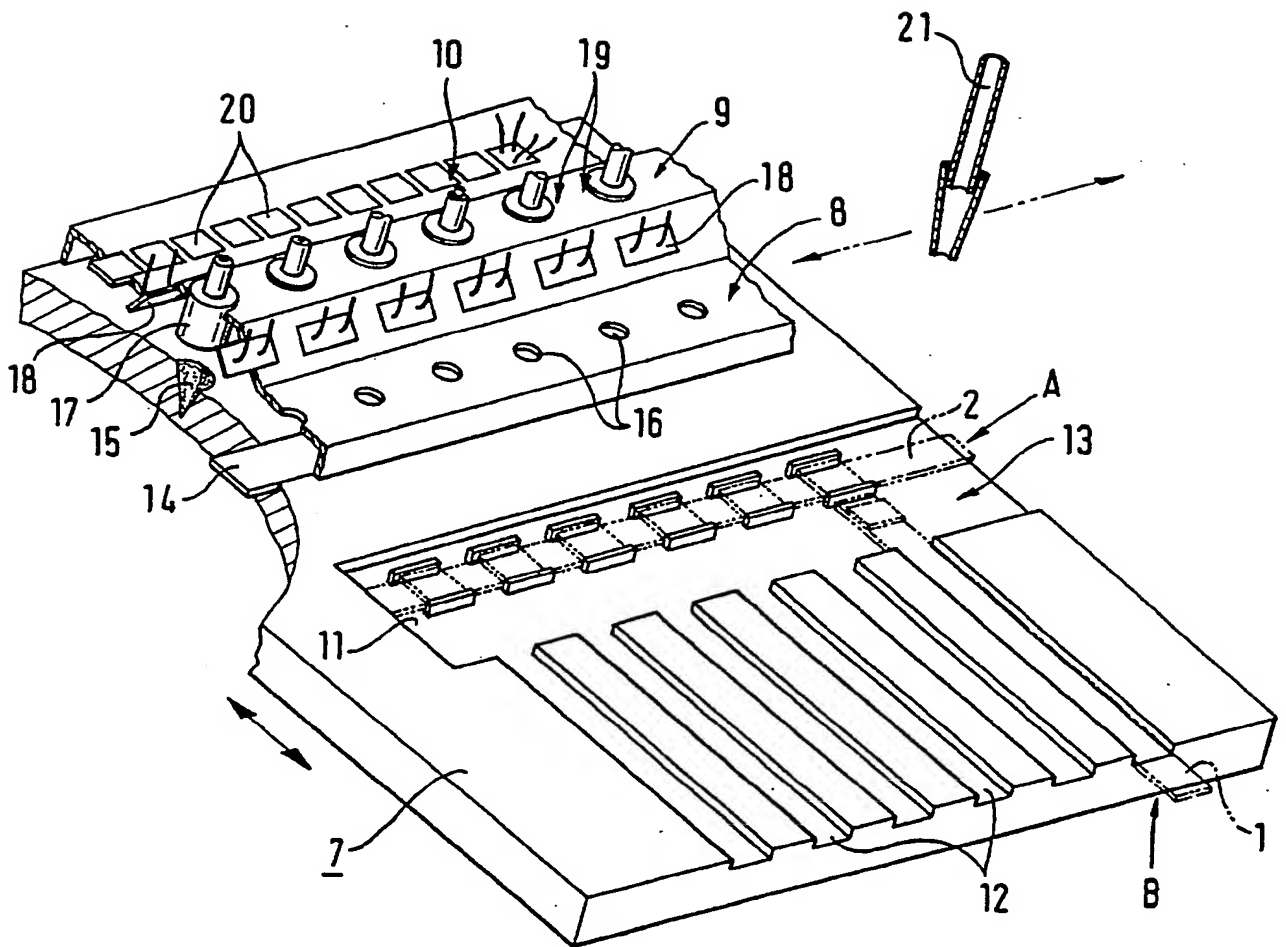


Fig. 3

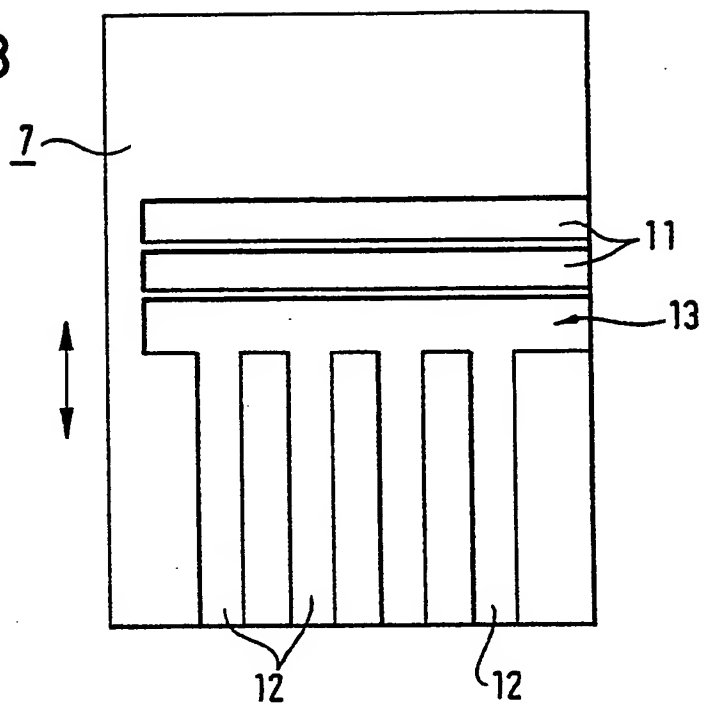
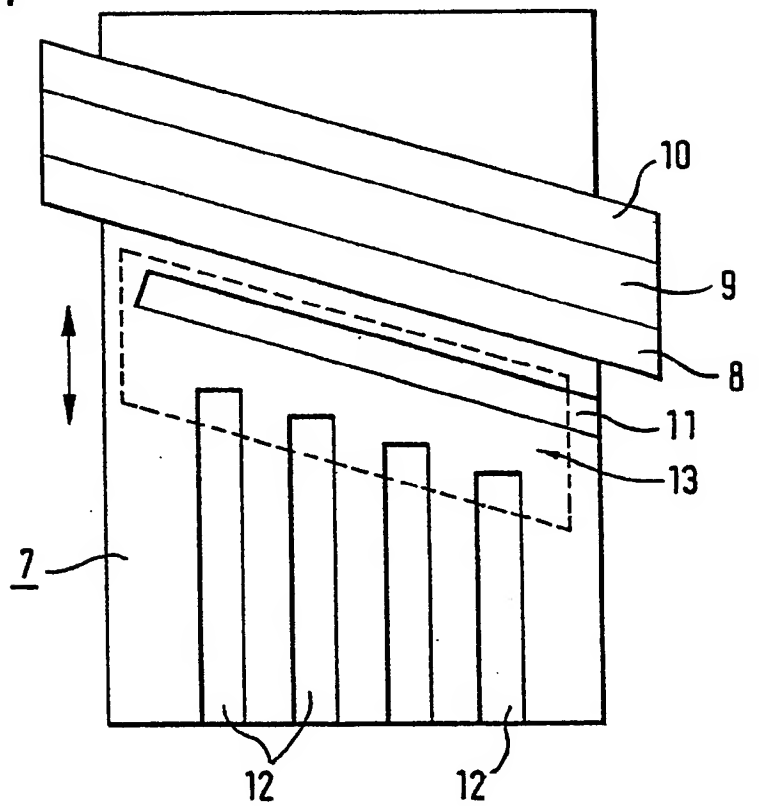


Fig. 4





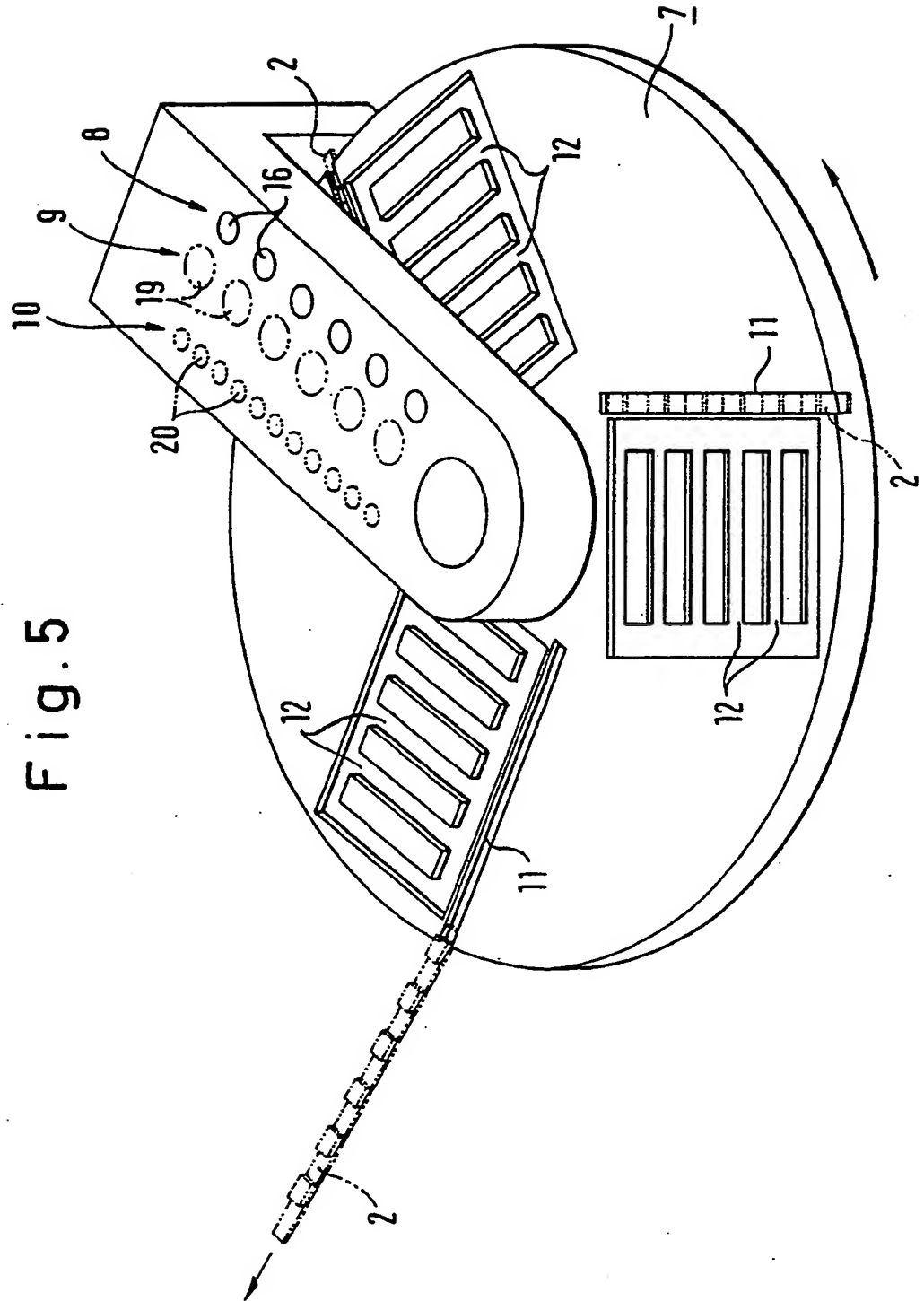


Fig. 5

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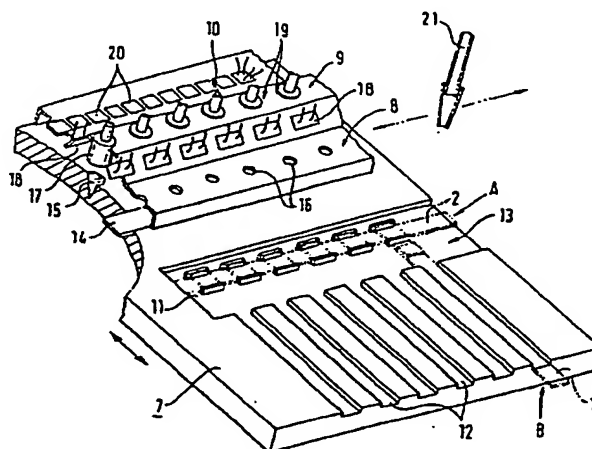
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54 **A method for analyzing special component in liquid.**

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Multi-item test piece is fed sideways to light receiving part, and single item test piece is fed lengthways to light receiving part.

Fig. 2



**EP 0 286 101 A3**



DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
A	EP-A-0 180 792 (Kabushiki Kaisha Kyoto Daiichi Kagaku) * Fig. 1; p. 21, l. 5-15 *	1,3	G 01 N 21/47 G 01 N 35/00 G 01 N 21/86
A	FR-A-2 361 651 (Olympus Optical) * Fig. 44,45; p. 53, l. 29 - p. 56, l. 7 *	1,2	
A	FR-A-2 378 277 (Kabushiki Kaisha Kyoto Daiichi Kagaku) * Fig. 4,5; p. 7, l. 30 - p. 9, l. 8 *	1,3	
X	US-A-4 592 893 (Poppe et al.) * Fig. 2; c. 2, l. 16-45 *	4	
A	PATENT ABSTRACTS OF JAPAN, vol. 9, no. 296 (P-407)[2019], 22. Nov. 1985 JP-A-60 133 359 (Fuji Sashin Film K.K.) 16.7.1985 * Whole document *	4	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
			G 01 N
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 17-01-1990	Examiner ZINNGREBE U.
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